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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/868,131	04/11/2002	Philip Cohen	022.00160	5850

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EXAMINER	
SAIDHA, TEKCHAND	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 02/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/868,131	COHEN ET AL.	
	Examiner	Art Unit	
	Tekchand Saidha	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 January 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-50* is/are pending in the application.

4a) Of the above claim(s) *2,4,5,11-43,45-47,49 and 50* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3, 6-10, 44 & 48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. ***Election***

Applicant's election of group I (claims 1, 3, 6-10, 44 & 48) without traverse in response to restriction requirement filed January 7, 2005, is acknowledged.

2. Claims 2, 4-5, 11-43, 45-47 & 49-50 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

3. This application filed under 35 USC 119(e) lacks the necessary reference to the prior application. This application claims the benefit of US Provisional Application No. 06/112,217, filed December 14, 1998, should be entered following the title of the invention or as the first sentence of the specification. Also, the present status of all parent applications should be included.

4. ***Priority***

Acknowledgment is made of applicants' claim for priority based on an application filed in United Kingdom on August 19, 1999.

5. ***Sequence Rules***

The instant specification – ***for example*** on page 2, line 24; pages 6-8, 10-11, 16, 20, 26-29, 38, 40-41, 66-67, 72, 85, 86, 97 and so on; Figures 1, 11-13; and Table 2 (pages 94-95) --- present amino acid or nucleotide sequences that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2), but fails to comply with the requirements. According to 37 CFR 1.821-825, every disclosed amino acid sequence of four or more residues or 10 or more nucleotides must be identified by a SEQ ID NO. The amino acid sequences presented do not have SEQ ID NOs. In order to comply with the sequence rules Applicants must identify these sequences by providing SEQ ID NO: ?, and where required provide a new version of the sequence listing and disk.

Specifically, Rule 1.822(e) requires the use of three letter abbreviation for amino acids.

New Sequence Rules

Since the effective filing date after July 1, 1998, Applicants should follow the New Rule Format and submit a new Sequence Listing (both in electronic and paper format). Compliance according to the requirements of 37 CFR 1.821 through 1.825 is required.

NOTE: Applicant's cooperation is requested in spotting all such amino acid and nucleotide sequences through out the specification and complying with the sequence rules.

6. ***Specification***

(a) The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

(b) The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

7. Group I claims 1, 3, 6-10, 44 & 48; & pertaining to a method of activating serum and glucocorticoid-induced protein kinase (SGK), wherein SGK is phosphorylated by 3-phosphoinositide dependent protein kinase-1 (PDK1); are under consideration in this examination.

8. ***Claim Objections***

Claims 44 & 48 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claims 44 & 48 depend upon claims not under

consideration. Placing the claims in proper dependent form will overcome this objection.

9. ***Claim Rejections - 35 USC § 112*** (first paragraph)

Written Description

Claims 1, 3, 6-10, 44 & 48 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1, 3, 6-10, 44 & 48 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims are directed to a method (or use of) of using a genus of polypeptide molecules having no defined structure.

Claims 1, 3, 6-10, 44 & 48 are rejected under this section of 35 USC 112 because the claims are directed to a method of using a genus of polypeptides comprising serum and glucocorticoid-induced protein kinase (SGK) wherein the SGK could be any variant including SGK1, SGK2, SGK3, SGKα or SGKβ, wherein the SGK is phosphorylated by PDK1 or a variant , fragment, fusion or derivative thereof or a fusion of a said variant, fragment or derivative, wherein none of the structures are apparent and none of the modifications claimed are disclosed in the specification (claims 1, 3, 6, 10, 44 & 48). This situation is further worsened since the discloser of the sequences lack sequence identifier numbers as well as a clear recitation or labeling of the named SGK or PDK sequences to their corresponding SEQ ID Nos. No description has been provided of the modified polypeptide sequences encompassed by the claim. No information, beyond the characterization of certain SEQ ID Nos: ? have been provided by applicants which would indicate that they had possession of the

claimed genus of hereto undiscovered modified polypeptides. The specification does not contain any disclosure of the function of all the polypeptide sequences derived from SGK or PDK variants, fragments, derivatives; or residues equivalent to Thr256 or Ser422 of full length human SGK-1 (claims 7-9), including variants within the scope of the claimed genus. The genus of polypeptides used in the method claims is a large variable genus including variants, fragments or fusion thereof which can have a wide variety of functions and which remain undescribed. Therefore many functionally unrelated polypeptides are encompassed within the scope of these claims. The specification discloses full length functional species [SEQ ID NO: ??] of the claimed genus, which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that applicant had possession of the claimed invention at the time the instant application was filed.

10. ***Enablement***

Claims 1, 3, 6-10, 44 & 48 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of activating human serum and glucocorticoid-induced protein kinase (SGK1) at Thr256 or Ser422 by phosphorylating with 3-phosphoinositide-dependent protein kinase-1 (PDK1) having the sequence(s) of SEQ ID NO: ?, does not reasonably provide enablement for a method of activating and phosphorylating using any SGK or PDK1 from any source or wherein the SGK or PDK has been modified in order to make a variant, fragment, fusion or derivatives thereof (claims 1, 3, 6, 44 & 48) or phosphorylating residues equivalent to Thr256, Ser422 (claims 8-10). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of protein kinases or SGK or PDK broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide and encoded amino acid sequences of the isoforms of glucocorticoid-induced protein kinase (SGK) and PDK1 for phosphorylating the SGK or isoforms thereof.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for these kinases from any source and further subject the kinases to multiple substitutions or multiple modifications in order to create variants, fragments of any size, fusion proteins or derivatives thereof, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions. Further derivatization or making fragments of undefined size will be highly unpredictable as no guidance is provided to the making of such modified SGK or PDK1. While it has been long established that protein kinases in general and p70 kinase in particular [Current Biology 1997, 8: 69-81] are activated *in vivo* through phosphorylation of serine and/or threonine residues; and PDK1 is shown to phosphorylate and activate protein kinase B (PKB, also

known as c-Akt). The ability of PDK1 to phosphorylate p70 Thr252 was strongly dependent on the phosphorylation of the p70 non-catalytic carboxyl-terminal tail (amino acids 422-525) and of amino acid Thr412 [see abstract, background on page 69, column 1-2, and the entire article). In view of this it is would be highly unlikely for a skilled artisan to determine how a fragment (which may be a di-peptide) or non-specific variant of PDK1, will be functional be effective in activating and/or phosphorylating SGK or fragment, variant or fusion protein thereof.

The specification does not support the broad scope of the claims which encompass a method using modified proteins of any SGK/PDK because the specification does **not** establish: (A) regions of the protein structure which may be modified without effecting SGK/PDK activity; (B) the general tolerance of SGK/PDK to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any SGK/PDK residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including a method for activating serum and glucocorticoid-induced protein kinase (SGK) and phosphorylating with any variant of PDK-1. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, developing a method such a that claimed, is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

11. ***Claim Rejections - 35 USC § 112*** (second paragraph)

Claims 7-9 & 44 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 7-9 recite 'residues equivalent to Thr256 or Ser422 of full length human SGK1'. The claims are indefinite because it is unclear what residues will be equivalent to what residues, as no specific SEQ ID NO: is used as a reference, nor clear equivalency of a residue in one sequence to another residues in another sequence has been established. Applicants' Figure 13, shows an alignments of amino acid sequences of SGK isoforms. However, Applicants have made no attempt to establish equivalency of the amino acid residues by numbering.

Claim 44 is included in the rejection for failing to correct the defect present in the base claim(s).

12. Claims 6 & 48 provides for the use of a PDK1 or a variant or use according to ..., but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 6 & 48 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

13. Claim 6 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

All claims are drawn to or are dependent upon claims that recite – 'A method of activating.....wherein the SGK is phosphorylated'.

Claim 6, lines 2-3, recites '...method of activating and/or phosphorylating SGK'. The claim is indefinite because the two processes do not occur in the alternate. Therefore, 'and/or' must be replaced by 'and', to overcome this rejection.

14. ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3, 6-10, 44 & 48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Alessi et al. [Current Biology 1997, 8: 69-81], and further in view of known human serine/threonine protein kinase sequence(s) of accession no. Y10032 [Waldegger et al.PNAS, USA., 94(9): 4440-4445 (1997).

Alessi et al. teach the general concept that protein kinases in general and p70 kinase in particular [Current Biology 1997, 8: 69-81] are activated *in vivo* through phosphorylation of serine and/or threonine residues; and where **PDK1** is shown to phosphorylate and activate protein kinase B (PKB, also known as c-Akt) or p70 kinase. Activation of p70 is dependent upon phosphorylation of at least 2 sites in addition to Thr252, namely, Thr412 and Ser394. Activation was achieved by phosphorylation of the serine/threonine protein kinase – namely, p70. [see abstract, background on page 69, column 1-2, and the entire article).

Alessi et al. do not teach serum and glucocorticoid-induced protein kinase [SGK]or any SGK or human SGK1]. Applicants have designated Human SGK as 'human SGK1'.

Accession No. Y10032 [PNAS, USA., 94(9): 4440-4445 (1997)], is described as a human *skg* gene, serine/threonine protein kinase. The translated protein sequence is also given [CAA71138.1], in the EMBL-EBI sequence information provided here, and which is attached to the PNAS paper.

Thus from the knowledge available in the teachings of the prior art as described above, it would have been obvious to one having ordinary skill in the art at the time the invention was made to use the existing method of the Alessi et al. of PDK1 phosphorylating and activating the general class of serine/threonine protein kinases by substituting a human SKG [orSKG1] for p70, and do so with a reasonable expectation of success. SKG, being a putative serine/threonine protein kinase, and as the name implies, serine or threonine residues in the amino acid chain would have been obvious sites to phosphorylate. One of ordinary skill in the art would have been motivated to make this substitution in view of the knowledge and known potential of developing a method for activating SGK by phosphorylation in order to better under the components of the signaling pathway [Alessi et al., conclusions], leading to developing strategies for better understanding and controlling signaling mechanisms associated with cellular function [Waldegger, PNAS, USA, 94: 4440-4445, 1997; see columns 1-2]. Thus, the claimed invention was within the ordinary skill in the art to make and use at the time was made and was as a whole, *prima facie* obvious.

15. No claim is allowed.

16. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the

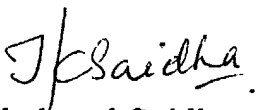
specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Similarly, based upon PCT search report, Applicants have filed three references. However, unless these references are listed in form PTO-1449, they have not been considered.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tekchand Saidha whose telephone number is (571) 272 0940. The examiner can normally be reached on 8.30 am - 5.00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (571) 272 0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



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